Department of Health and Social Security
Department of Health and Social Services, Northern Ireland
Scottish Home and Health Department
Welsh Office

Third Report of the Independent Scientific Committee on Smoking and Health

Chairman: Dr Peter Froggatt, MD PhD LLD DSc FFCM FRCP

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25 January 1983

The Rt Hon Norman Fowler MP
Secretary of State for Social Services
Department of Health and Social Security
Alexander Fleming House
Elephant and Castle
London SE1 6BY

Dear Secretary of State

I have the honour to present the Third Report of the Independent Scientific Committee on Smoking and Health.

This Report considers further the major issues relevant to the development of "less harmful" cigarettes: these were mentioned in the Second Report of the Committee and referred to in more detail in my predecessor's letter of 5 December 1979. The Committee is unequivocally of the view that smoking should be discouraged. We recognise, however, that despite advice some people will take up smoking and some smokers will continue to smoke and we therefore believe it is important that such people should be enabled and encouraged to smoke less harmfully. We have been conscious, in preparing our Report, that our recommendations will form the basis for negotiations between Government and the tobacco industry on a further agreement on product modification. We hope that those negotiations will concentrate on the most practical ways of achieving our recommendations since we believe these to be consistent both with the need to reduce the harmful effects on health of smoking, and with commercial practicalities. In this respect we were disappointed that the recommendations in my predecessor's letter of 5 December were not implemented in full by the current voluntary agreement.

We attach great importance to the need for research intended to demonstrate the effects on human health of product modification and we are grateful therefore to the tobacco industry for providing us with £3 million for this purpose. Indeed, I am pleased to say that we maintain a fruitful working relationship with the industry and derive great benefit from our continuing discussions both with the industry as a whole and with individual companies.

I would wish to pay tribute to my predecessor, the Lord Hunter of Newington, who guided the work of the Committee with skill and studious care for seven years. My thanks are due to all my colleagues on the Committee for the commitment and expertise they have brought to the Committee's business, and to the members of the secretariat for their conscientious skill.

I am, Secretary of State,

Your obedient servant,

Peter Froggatt.

(Chairman, Independent Scientific
Committee on Smoking and Health)

The Secretary of State for Social Services
The Secretary of State for Scotland
The Secretary of State for Wales
The Secretary of State for Northern Ireland

INTRODUCTION

1. Our first report(1) dealt with the testing and marketing requirements of tobacco substitutes and tobacco additives. Our second(2) contained details of further work carried out by the Committee in relation to these matters, including revised guidelines for the testing of substitutes and additives, and outlined initial progress in the development of 'lower-risk' cigarettes. This third report considers the development of 'less harmful' cigarettes and comments on the current state of knowledge of the major noxious components of tobacco smoke. (For details of our terms of reference and membership, see Appendices I and II.)

2. On 5 December 1979, our Chairman at that time wrote to the Secretaries of State setting out our preliminary conclusions and recommendations on these points, and these formed the basis for discussions on the product modification provisions of a new voluntary agreement between the Government and the tobacco industry announced on 21 November 1980. (For the text of the Chairman's letter see Appendix III.) Not all our recommendations, however, were incorporated in that agreement which, in respect of the provisions relating to product modification, will run until 31 December 1983.

3. We welcomed a provision in the agreement under which the tobacco industry agreed to provide up to £1 million per annum for independent monitoring research, as proposed by us, into the effects of product modification. Following discussions with the industry a charitable trust has been set up to administer this research fund and the industry is from December 1981 paying £250,000 each quarter to the trust until a total of £3 million has been paid. We wish to record our appreciation of the industry's constructive and helpful approach in this matter.

4. This report discusses separately each of the five major issues considered to be relevant to the development of 'less harmful' cigarettes. Briefly, these are:

- i. the role played by 'tar'* in lung cancer and reduction in tar yields (paras 7–11);
- ii. the role of nicotine in smoking-related diseases and in the smoking habit and the level of nicotine yields (paras 12–20);
- iii. the role of carbon monoxide in ischaemic heart disease and peripheral vascular disease and the reduction of carbon monoxide yields (paras 21–25);
- iv. investigations of components other than tar, nicotine and carbon monoxide, ie 'other noxa' (paras 26–27); and

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* 'tar'—defined as 'That portion of the whole smoke which is retained in a Cambridge filter smoke trap corrected for its contents of water and nicotine alkaloids (expressed as mg/cigarette)'.

v. monitoring effects on health of the modified smoking products (paras 28–33).

We comment also on passive smoking (paras 34–35) since inhalation of sidestream smoke has been considered by some to be harmful and product modification will affect the yields of noxa in sidestream as well as mainstream smoke.

Tobacco substitutes and additives

5. Before turning to these major issues we make the following points concerning tobacco substitutes and additives:

i. Cigarettes containing substitutes command only a negligible section of the market: this failure of market penetration frustrated the execution of the planned large scale epidemiological study referred to in paragraph 9 of our Second Report(2). We maintain our view that if the tobacco industry wishes to continue to market tobacco substitutes then long-term human health studies must be carried out to assess the effects of these modified products. Meanwhile we intend, if possible, to include a group of people smoking tobacco substitutes as part of our proposed studies investigating respiratory and cardiovascular symptoms (paras 30 and 31).

ii. The system of submitting information on additives not currently permitted in products to be marketed in the UK has been working well (para 14 of Second Report(2)). We recommend that this system continues.

6. We have reconsidered paragraph 17 of our Second Report(2)—in which we stated that manufacturers could continue to use additives in components such as cigarette papers, filter wrappers, tips and overwrappers without reference to us—because of the amendment to the Poisons Rules on 1 April 1982 permitting the addition of a specific salt of nicotine to cigarette papers. We now consider that our role in the evaluation of additives should be extended to include assessment of all substances to those parts of tobacco products intended to be burnt. We would wish therefore to receive submissions on all new additives in cigarette papers through a procedure similar to that used for other tobacco additives (Appendix VI of our Second Report(2)). Additives currently used in cigarette papers may continue to be used but we would wish to receive information about these in order to compile an historical list as for other tobacco additives. Tips, filters, filter wrappers and overwrappers are not intended to be burnt and additives in these components may therefore continue to be used without reference to the Committee.

TAR

7. We have reviewed the epidemiological data which associate lung cancer and chronic obstructive lung disease with cigarette smoking(3–7). Human data, acute and chronic *in vivo* studies in animals(8–12) and short-term *in vitro* toxicity studies lead us to concur that tar is the major tobacco component in lung cancer causation. Death rates from lung cancer are now declining among men at all ages up to 75(13). The interpretation of such trends is complicated because of changes in both the quantity and composition of cigarettes smoked and the confounding effect of other environmental factors, but the decline is most marked in the younger age groups whose smoking experience, compared to the older age groups, will have been influenced more by the lower-tar cigarettes available during the past 20 years. Among women, lung cancer death rates continue to rise overall, but, despite increases in the relevant lifetime consumption of cigarettes, death rates appear to be levelling off at ages up to 50, again suggesting the impact of a reduction in tar yields.

8. We believe that further reductions in the tar delivery of cigarettes should maintain the downward trends in lung cancer mortality though we cannot make precise predictions since we do not know the form of the relationship between the incidence of lung cancer in smokers and the levels and duration of smoke exposure. Furthermore we must maintain our consistently expressed view that no dose of tar can be considered entirely safe. We welcome the reduction in sales-weighted tar yields achieved by the industry so that by the end of 1983 the sales-weighted average tar yield will be under 15 mg/cigarette. Whilst rapid changes in tar yields would be highly desirable for health reasons, we recognise that we must take account of consumer acceptability in making our recommendations. We therefore recommend that over the four years 1984–1987 reduction in the sales-weighted tar delivery should continue at the same rate as set in the 1980 voluntary agreement for the period 1979–1983. This will produce an average tar yield of approximately 13 mg/cigarette by the end of 1987. We have also considered the maximum tar yields of new brands of cigarettes introduced onto the market and we recommend that in future every new brand should deliver less than 13 mg tar/cigarette. Paragraph 13 of our Second Report(2) recognised the potential value of the use of flavouring additives in improving the acceptability of lower tar cigarettes to the smoker and we will continue to approve the use of those against which there is no evidence of increased hazard.

9. We have noted that, with the reduction in tar yields, the numbers of cigarette brands appearing in each of the tar groups defined by the Government have become very unequal with the greatest number of brands now appearing in the Middle Tar group. We recommend that the definition of tar groups be reconsidered.

10. The carcinogenic effects of tobacco smoke have been related to the content of the tar fraction as a whole. This fraction contains small amounts of recognised carcinogens but their levels seem unlikely to account for all the cancer risk attributable to cigarette smoking. Producing a 'less harmful' cigarette with respect to the tar fraction must involve reduction in whole tar yield but in addition selective reduction of constituents must be considered where components, which might have carcinogenic effects, occur at higher yields.

11. The level of tar in cigarettes may be associated with smoking-related diseases of the respiratory tract other than lung cancer, one category of which includes chronic bronchitis and obstructive lung disease. We recommend research into this possible association. In addition we note the lack of information on the role of tar in the acceptability of cigarettes to the smoker and we would like to receive any relevant data the industry may have.

NICOTINE

Nicotine and its role in smoking-related diseases

12. We have reviewed the extensive literature relating to the administration of nicotine in animals and man over a wide range of doses. Studies report various effects of nicotine such as nausea, vomiting, sweating, and increases in heart rate, blood pressure and cardiac output. Most of these effects, however, are produced at levels of nicotine well in excess of those achieved by smoking. The nicotine in a cigarette of 1 mg yield spread over the normal period of smoking will produce at most only minor changes in blood pressure and heart rate(14) of an order well within the normal daily physiological variation.

13. Small doses of nicotine may, however, be harmful to people with certain disease states, most particularly ischaemic heart disease and peripheral vascular disease(15, 16). Whilst we wish to discourage everyone from smoking this applies particularly to those with impaired cardiovascular or peripheral vascular function. We recommend further investigation into the effects of nicotine at the levels achieved through smoking.

14. There is no evidence that nicotine, at levels obtained from smoking, is teratogenic(17, 18). Maternal smoking can, however, be harmful to the foetus in other ways: it is associated with low birthweight and reduction in foetal movement, and when the mother is smoking the foetal heart rate increases and the placental blood flow falls. The responsible component or components have not been identified but nicotine has not been excluded. Furthermore, nicotine is present in the breast milk of lactating smoking mothers(19, 20). Therefore over and above our general recommendation (para 13) expectant and nursing mothers should be discouraged from smoking.

15. The carcinogenic potential of nicotine at levels experienced by smokers has never been adequately studied. Many investigations have used doses of nicotine far beyond those experienced by smokers and their duration has rarely been longer than six months. The results, however, indicate clearly that nicotine is not a potent carcinogen and there is no convincing evidence that it is even weakly carcinogenic(21,22). Nor is there consistent evidence implicating nicotine as a co-carcinogen, though this requires further investigation. From *in vitro* studies nicotine is known to be a precursor of nitrosonornicotine (NNN) and 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK). Both of these substances have been detected in tobacco and tobacco smoke(23) and have been shown to cause oesophageal tumours, lung adenomas and nasal cavity tumours in laboratory animal studies(24,25,26), but the relevance of these studies to smoking in man is doubtful. Until adequate contrary evidence becomes available nicotine and its metabolites must be considered to play little or no role in carcinogenesis.

Nicotine and the smoking habit

16. There are many reasons why people start to smoke but dependence on nicotine is probably the most important single reason for their continuing to smoke. What nicotine offers to the smoker has yet to be fully explained. It undoubtedly induces dependence affecting psychological, emotional and cognitive functions (though it does not markedly affect physiological functions). It may modify sensory perception, eg taste and smell and it can improve performance in tests requiring vigilance and enhance attention and concentration during prolonged tasks. Furthermore it may improve attainment in information-processing, such as mental arithmetic and in learning ability, and may even alter mood by decreasing anxiety and anger. The evidence for many of these effects comes from tests which are relatively crude compared with the complexity of human behaviour(27,28). In short, the role of nicotine in perpetuating the smoking habit is imperfectly understood and we recommend that further well-conducted studies be undertaken at the relevant lower range of nicotine dosage.

17. We have noted that the sales-weighted nicotine yields of cigarettes fell *pari passu* with tar yields until 1972 since which time they have remained relatively constant, largely by selective incorporation of high nicotine tobaccos. Our recommendation in paragraph 8 of this report is that tar yields should fall even further. This may result in a further reduction in nicotine levels (though we make no specific recommendation on this point). The industry has told us, however, that the level of nicotine in some cigarettes has already reached a point where consumers are trying to maintain their nicotine intake by methods of 'compensation': these include increases in puffing, depth of inhalation and cigarette consumption, and changing brands. If such 'compensation' took place

to a substantial extent this could compromise our main recommendations which relate to a reduction in the lifetime intake of toxic substances in tobacco smoke by reducing both the yield of such substances from each cigarette smoked and the total of cigarettes smoked. As the levels of sales-weighted tar and nicotine yields decrease so the importance of monitoring 'compensation' increases.

18. We have reviewed the available information concerning these changes in smoking practice(29–39) and conclude that further investigations are necessary since most of the studies are unsatisfactory for our purpose. We would seek evidence from the industry on the number of cigarettes smoked by smokers who have either changed to cigarettes with reduced yields or who regularly smoke brands of cigarettes whose yields have been reduced significantly over time. We also require evidence about changes in the manner of smoking which may increase the absorption of toxic substances per cigarette; current information is inadequate and the problem should be investigated further by the industry over extended periods of smoking (after short-term adaptation) and using larger and more appropriate groups. We consider that the evidence so obtained could be important in advising on the future development of the product modification programme. We would wish to discuss the design of such studies with the industry.

Future nicotine yields

19. In summary: nicotine, at the levels derived from smoking, has not been shown to harm the cardiovascular system in healthy people, nor has it been shown to be either carcinogenic or teratogenic. Even in these doses it may, however, exacerbate existing cardiovascular and peripheral vascular disease in people at risk and it has been found in breast milk. Nicotine also produces dependence. Cigarette smoking *per se* is associated with many excess deaths from cardiovascular disease as well as from respiratory disease but we do not know what component or components in the tobacco are responsible. We cannot predict the effect on either cardiovascular or total deaths of further reductions in nicotine.

20. As nicotine is an important factor in perpetuating the smoking habit and as the evidence is not convincing that the lower limit of nicotine acceptability has been reached we wish to encourage a lower nicotine intake on the ground that this will reduce dependence on tobacco and thus help smokers to give up. Additionally, there is no clear evidence of marked compensation over long periods; so even accepting that some may occur, the lowering of tar and nicotine yields would still result in reduced average intakes of these substances. We accordingly recommend that, in general, nicotine levels should fall. We also believe that there should be available to the public some brands with tar yields below those of the present principal Low Tar brands (ie below about 8

mg/cigarette), but with proportionately higher nicotine yields (up to about 1 mg). There should be careful monitoring of public acceptance of such brands, and of the extent of 'compensation' both in those who use them and in those who smoke more conventional low tar cigarettes.

CARBON MONOXIDE

21. Everyone is exposed to carbon monoxide from endogenous and environmental sources but for smokers the main source of carbon monoxide is their own tobacco smoke. The carbon monoxide yields of cigarettes currently tested by the Laboratory of the Government Chemist range from 0.5 to 18.5 mg/cigarette. For 1981 the Laboratory of the Government Chemist estimated the mean sales-weighted yield of all brands to be about 15 mg/cigarette. The overall correlation between tar and carbon monoxide yields is low in contrast to the relatively high correlation between tar and nicotine yields. Cigarettes low in carbon monoxide are predominantly those incorporating into the design characteristics highly porous paper and/or ventilated filters.

22. We have evaluated the reported effects of carbon monoxide in man and animals. In man, there is a close relationship between carbon monoxide exposure and blood carboxyhaemoglobin levels(40) both in smokers and non-smokers. Epidemiological evidence shows that certain cardiac and peripheral vascular conditions are associated with smoking. Carbon monoxide is suspected of having a role in their development but it is not clearly established that it is a factor in their causation(3, 31–43). Furthermore, many of the studies have not been rigorously designed(44–49): more suitable studies are required and these would need to take account also of other substances found in tobacco smoke.

23. Carbon monoxide can lead to attacks of angina pectoris in those already susceptible(50–52) but there is no clear evidence of any such effects in smokers not already predisposed to such attacks. Moderately raised carboxyhaemoglobin levels, within the range that can be reached through smoking, have been associated with small decrements in the performance of tasks requiring concentration but the results of such studies are equivocal(53, 54). Other components of tobacco smoke, such as nicotine, may have opposing effects on the ability to concentrate (see para 16) and further research in this area is also required.

24. We conclude that there are sufficient health grounds to require substantial reductions in carbon monoxide yields of cigarettes. We have therefore sought advice on whether such reductions are practicable and whether they could be achieved without loss of brand acceptability which could result in smokers moving to other, perhaps more harmful, brands. We are advised that reductions

of the order required are technically feasible within the product modification programme even though carbon monoxide and tar yields are reduced in not-necessarily equal proportions by different techniques. Carbon monoxide in doses now yielded by cigarettes leaves no taste and its presence in smoke has no advantage to the smoker. Reducing carbon monoxide, however, will also *pari passu* reduce the yields of other gaseous components such as nitrogen oxides: this could affect the taste and hence consumer acceptability but we are advised that this potential problem is not insuperable. Some of the gaseous components so reduced may be harmful (see para 26) and this would be a distinct additional advantage of any programme to reduce carbon monoxide yields.

25. An early and substantial reduction in carbon monoxide yields is practicable, may have important benefits for health in those with certain cardiac, pulmonary or peripheral vascular diseases, and is without serious disadvantage. Accordingly we recommend that

i. manufacturers should reduce carbon monoxide yields of all brands of cigarettes to the lowest practicable values;
ii. no new brands should be introduced with carbon monoxide yields exceeding the current (1981) estimated sales-weighted mean for all brands of about 15 mg/cigarette;

and

iii. the industry should provide the Health Departments with information on sales-weighted carbon monoxide yields in the same way as they already do for tar.

We have already advised the Secretaries of State that carbon monoxide yields of cigarettes should be published together with those for tar and nicotine.

OTHER NOXA

26. In addition to tar, nicotine and carbon monoxide, there are many other components which may contribute to the health hazards of smoking. We have reviewed some of those often considered to be associated with carcinogenicity, ciliotoxicity or to have an effect on the heart(18, 55) but in general there is insufficient evidence to incriminate individual compounds, at the levels occurring in smoke. Many of these components will be reduced *pari passu* with product modification and especially by our proposals for reductions in carbon monoxide yields and we would not at this stage recommend the selective removal or reduction of any of them. Research should, however, be conducted into the possible toxicity of certain of them in the context of whole smoke and, if appropriate, towards their selective elimination.

27. To further research in this area, the Committee would welcome industry's agreement to set up a collaborative research committee to investigate such

components. We would wish to hold discussions with the industry to formulate acceptable objectives. Of major importance, and in need of particular examination are the roles of the following:

- i. acrolein, formaldehyde and hydrogen cyanide in relation to ciliotoxicity and pulmonary clearance;
- ii. cresols and phenols in promoting carcinogenesis;
- iii. polycyclic aromatic hydrocarbons (PAHs) and nitrosamines in relation to carcinogenicity;
- iv. nitrogen oxides in relation to respiratory diseases;
- v. the interrelationship of hydrogen cyanide and carbon monoxide with levels of haemoglobin and haematocrit values;
- vi. acetaldehyde for its effects on the heart.

We recognise that in addition to the above, many other components may play a role in the hazardous effects of smoke. An exhaustive list cannot readily be compiled as many components remain to be identified, but of the known constituents the list would include, for example, silica, cadmium, nickel, ammonia and polonium-210.

MONITORING OF THE HEALTH RISKS OF MODIFIED SMOKING PRODUCTS

28. As part of the Voluntary Agreement of 21 November 1980 between UK Health Ministers and the tobacco industry, the latter agreed to continue its long-standing policy of reducing the tar yield of cigarettes. We support this policy. In order to help determine whether it does in fact result in a 'less harmful' cigarette the industry agreed to provide up to £1 million per annum, for 3 years, for 'independent monitoring research', as proposed by the Committee, into the effects on human health of product modification. Because a smoker's choice of tobacco product is liable to be affected by his existing symptoms or general response to the smoke, it is essential to conduct interventional studies in which the smokers are allocated at random to two or more groups and required to smoke particular products differing in yields mainly of tar but possibly also of other constituents and in which their subsequent mortality and morbidity are noted. Such studies are technically and operationally difficult and need to be accompanied by appropriate studies in which the mortality and morbidity of a large group of individuals are observed in relation to their chosen, ie self-determined, smoking habits. The Committee is still considering proposals, but an outline of the types of studies envisaged is given below.

29. A general observational study could examine trends and contrasts in smoking-related diseases between sub-groups of the population defined for example, in terms of geographic region or social class, making use of nationally-

collected data on mortality, cancer registration and morbidity. Detailed information on smoking habits classified by brand or tar range would be required to link with the health indices. A more satisfactory, but much longer-term, approach could be to embark on a prospective survey among a large sample of the population, recording each person's smoking habits and subsequent mortality. As an intermediate step hospital based case/control studies of the type originally undertaken to investigate the relationships between smoking and lung cancer could be carried out, provided reliable histories of amounts and types of cigarettes smoked could be obtained from the patients.

30. The experimental ('intervention') studies under consideration include one to investigate changes in respiratory symptoms in relation to the type of product smoked. Suitably selected subjects unwilling to stop smoking and already smoking Middle (or Middle to High) Tar cigarettes would be invited to participate in the trial, being allocated to, say, Middle Tar and Low Tar groups. The ability of subjects to comply with their allocated regime and other features of the protocol would be tested initially in pilot studies.

31. A second type of intervention study to investigate cardiovascular effects of the same selected products is also being considered. Subjects would be drawn from groups, who are unwilling to give up smoking, and who have recovered from myocardial infarction or who have had evidence of arterial disease. A measure of effect might be the recurrence, severity, frequency or time interval of subsequent episodes of myocardial infarction or a worsening of their arterial disease. Ethical problems would need to be considered carefully before proceeding with such a study.

32. Thirdly it would be desirable to investigate whether smoking Low Tar cigarettes compared to higher tar ones leads to any reduction in smoking effects related to pregnancy, but the possibility of using an interventional approach has been rejected on ethical grounds.

33. In paragraph 18 we have expressed the desire for further information from the industry on the extent to which 'compensation' occurs when smokers change to a lower tar/nicotine product. Evidence on this point may emerge from the above studies, but if these prove not to be feasible, it may be necessary for us to commission studies specifically on compensatory smoking.

PASSIVE SMOKING

34. The smoke produced by smouldering tobacco (sidestream smoke) contains greater quantities of many smoke components than an equivalent weight of the smoke directly inhaled by the smoker (mainstream smoke). The question of whether passive smoking (inhalation of sidestream and exhaled mainstream

smoke) has any adverse effect on the health of the non-smoker, rather than being merely offensive, has been raised several times over the past few years but until recently there has been no real evidence to cause concern(56). Current restrictions on smoking in certain public places have been based on the habit being anti-social rather than on any health risk to non-smokers. However, with the recent publication of several reports investigating the incidence of lung cancer in the non-smoking wives of smokers we have considered the available evidence relating to the effects of passive smoking on the health of different age groups of the population.

35. Tobacco smoke can irritate the eyes, nose and throat(57). Children in early life exposed to tobacco smoke from parental smoking in the home have an increased incidence of respiratory illness(18, 56, 58–60). Passive smoking may exacerbate symptoms in adults already suffering from coronary and other arterial diseases and from chronic obstructive lung disease(52, 61). Some studies show that persons exposed, through passive smoking, to high concentrations of tobacco smoke have raised blood levels of carboxyhaemoglobin and nicotine though, as in smokers, it is not known whether such concentrations have any harmful effects on healthy adults(62, 63). Of four recent studies, two have suggested that passive smoking in adults is associated with an increased risk of developing lung cancer(64, 65); the results of a third(66), though suggesting no association, are not inconsistent with there being a weak association, while results of a fourth(67) suggest no association. We believe that many of the reported associations, including that between passive smoking and lung cancer, have not been established unequivocally: rigorously planned epidemiological and other studies are needed despite the obvious technical difficulties. We recommend that while further evidence accumulates the industry should pursue research into reducing the amount, irritancy and any other deleterious property of sidestream smoke.

CONCLUSIONS

36. Cigarette manufacture has been undergoing a period of rapid change. We are encouraged by the decrease in tar yields over the last few years and recommend a continued reduction. We have recommended that nicotine levels should, in general, continue to fall but that there should also be available to the public some brands with very low levels of tar and a proportionately higher nicotine yield though this should not exceed about 1 mg. We have proposed further reductions in carbon monoxide yields. Tar and nicotine, and more recently carbon monoxide, have been the only smoke noxa studied in any great detail with regard to their role in smoking-related diseases and we now look to co-operation with industry in exploring possible means of studying the effects on health of certain other noxa most of which, under our present recommendations,

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will be further reduced. It is important that we keep abreast of the rapid developments in cigarette manufacture and that we continue to monitor the consequences of product modification on health. In particular, evidence relating to 'compensatory smoking' could be important in advising on the future product modification programme.

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NB: The bibliography above relates only to those publications selectively referred to in the text of this report. In order to arrive at these conclusions a far greater number of papers was considered.

Appendix I

Independent Scientific Committee on Smoking and Health

TERMS OF REFERENCE

The Committee is appointed by the Health Ministers to advise them and, where appropriate, the tobacco companies on the scientific aspects of matters concerning smoking and health, in particular:

(a) i. To receive in confidence full data about the constituents of cigarettes and other smoking materials and their smoke and changes in these.
    ii. To release to *bona fide* research workers for approved subjects such of the above as is agreed by the suppliers of it.

(b) To review the research into less dangerous smoking and to consider whether further such research, including clinical trials and epidemiological studies, needs to be carried out;
and

(c) to advise on the validity of research results and of systems of testing the health effects of tobacco and tobacco substitutes and on their predictive value to human health.

Appendix II

Independent Scientific Committee on Smoking and Health

MEMBERSHIP

Dr Peter Froggatt
Vice-Chancellor, The Queen's University of Belfast, Belfast (Chairman from October 1980)
Professor Sir Ivor Batchelor CBE
Department of Psychiatry, Ninewells Hospital, University of Dundee (from May 1980)
Professor J R T Colley
Department of Community Health, University of Bristol (from March 1982)
Dr P C Elmes
Formerly Director, Pneumoconiosis Unit, Llandough Hospital, Penarth, Glamorgan (from May 1980)
Dr F A Fairweather
Unilever Research, Unilever House, London (from March 1982)
Professor R M Greenhalgh
Department of Surgery, Charing Cross Hospital, Fulham, London (from May 1980)
Professor W W Holland
Department of Community Medicine, St Thomas's Hospital Medical School, London (from March 1982)
Dr C G Hunter
Formerly of the Occupational Health Service, Kings College Hospital, Denmark Hill, London
Dr F Moran
Centre for Respiratory Investigation, Royal Infirmary, Castle Street, Glasgow
Professor A Neuberger CBE
The Lister Institute of Preventive Medicine, Charing Cross Hospital Medical School, London
Professor Sir William D M Paton
University Department of Pharmacology, South Parks Road, Oxford
Professor D E Poswillo
Royal Dental Hospital of London, School of Dental Surgery (University of London) (from May 1980)
Professor G A Rose
London School of Hygiene and Tropical Medicine, University of London
The Lord Hunter of Newington (Chairman until September 1980)
Vice-Chancellor, Birmingham University

Dr J D Ball
Llandough Hospital, Penarth, Glamorgan (until January 1980)
Professor Sir Theo Crawford
Pathology Department, St George's Hospital, London (until January 1980)

……

Chief Scientific Adviser:
Dr F A Fairweather, *Department of Health and Social Security* (until December 1981)
Chemistry Adviser:
Dr H Egan (until December 1981)
G F Phillips OBE (from January 1982) *Laboratory of the Government Chemist*
Secretary:
D Milner (until September 1980)
K J Guinness (from October 1980) *Department of Health and Social Security*
Scientific Secretary:
Dr A J Nelmes (until November 1980)
Mrs C A Swann (from July 1981) *Department of Health and Social Security*

Appendix III

The University of Birmingham
Chancellor's Court, P.O. Box 363, Birmingham B15 2TT
Telephone: 021-472 1301

From the Vice-Chancellor and Principal:
The Lord Hunter of Newington, DL LLD FRCP

5th December, 1979

1 In its Second Report to the Secretaries of State, the Independent Scientific Committee on Smoking and Health considered the progress made towards the development of "lower-risk" cigarettes. Subsequently the Committee has had wide-ranging discussions with the tobacco industry on the practicability of developing cigarettes which are less harmful to health. We have also been evaluating the evidence on tar, carbon monoxide and nicotine yields from cigarettes, and on the role of other noxa in smoke. A report on these findings is being prepared, but the size of the task is such that it will not have been completed before Health Ministers will have had to consider what should follow the present voluntary agreements with the industry when they expire in March 1980. However, in the light of the work it has done to-date, the Committee can now confidently make some recommendations about a positive course of action which willlead to the production of "lower-risk" cigarettes.

TAR

2 The Committee has reviewed the data which associate lung cancer, chronic bronchitis and heart disease with the consumption of cigarette tobacco. From this, and studies in animals, the Committee maintains that the major carcinogenic compounds reside in the 'tar' or particulate phase of the smoke. The results of recent epidemiological studies indicate a slight decline in mortality from cancer of the lung among men up to 75 years of age and a greater reduction among men under 45. These results, in our view, can be related to the reduced tar delivery of cigarettes over recent years, which has been brought about by public awareness of the risk to health from cigarette smoking and by the industry's efforts to reduce tar yields. Although uncertainty exists about the magnitude of risk from tar in relation to the dose, all the evidence indicates that if the decline in mortality from lung cancer is to be accelerated and not just maintained, it is vital that the 'tar' delivery of existing cigarette brands should continue to go down.

3 While it has not been possible to explain the total biological activity of smoke in terms of individual smoke constituents that have been identified, some condensate fractions and certain constituents have been implicated in the initiation and promotion of cancer. Further

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research into this multifactorial problem is needed to identify the particular components involved in carcinogenesis and until this has been done, the Committee believes that the reduction should be in whole 'tar'.

4 Since the mid-1960s, there have been significant reductions in the tar yield of cigarettes. The average sales-weighted yield per cigarette has fallen from 31.4mg/ cigarette in 1965 to 17.3 mg / cigarette in 1978. We see, in particular, a danger that too rapid a reduction in future could lead to rejection by smokers who would then revert to brands with higher 'tar' deliveries. We therefore think that a reasonable objective would be a substantial reduction (in the same proportion as has been achieved since 1972) in the next five years.

5 In practical terms, these reductions can best be achieved in two stages. First, there should be a further reduction in the tar yields of existing brands. The evidence from consumer acceptability studies which the Committee has seen, suggests that such reductions should be possible in the middle tar range by existing methods (perhaps including substitutes) without apparent loss of consumer appeal. Progress towards these reductions should, I suggest, be reviewed regularly. Also, any new brands introduced should in our view yield less than 15 mg / cigarette. Second, there should be a re-evaluation of cigarette design and ways sought to make yet further reductions in the 'tar' delivery and in the components of 'tar'. These may involve the use of blended, expanded or sheet tobacco based on stem, diluents such as substitute for tobacco, selective filtration and ventilation, possibly in combination with flavouring additives. The Committee will continue to evaluate such modifications.

6 We would not wish these quantitative reductions to obscure the need for qualitative changes, especially where there is evidence of relatively high yields of potentially toxic components and, as we have already said, when and if research identifies specific components as particularly responsible for carcinogenesis.

7 The determination of a rate of reduction in tar yields is, we recognise, a matter which rests between Health Ministers and the industry. My purpose in writing this letter is to give you, from the Committee's examination of present evidence, a scientific foundation on which Health Ministers can base their judgments. My Committee and I attach great importance, within the context of our work, to the need to secure reduction in tar yields. We hope that the objectives we recommend will be built into whatever general

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arrangements are made with industry to follow the present voluntary agreements. But they are, at present, only objectives. If they are to be translated into results it will be necessary to have a constant dialogue between the scientists in industry and those who serve my Committee. The industry recognise this, but because the information which will be needed is so closely concerned with commercial developments, this dialogue will be largely with individual companies and we shall have to ensure that confidentiality is fully respected in this highly sensitive area. Moreover, the industry will wish, before investing heavily in developing "lower-risk" cigarettes, to have some assurance that the results of their efforts (based on what my Committee considers sound scientific and appropriate data) will have from Government the kind of support which will not inhibit the commercial exploitation of their research. The industry have suggested that my Committee should regularly review progress on all scientific matters, but especially tar reductions. The advantages of this - not least in being able to provide Health Ministers with an up-to-date scientific basis for responding to questions - seemed self-evident and I am following up the suggestion with the industry.

CARBON MONOXIDE

8 My Committee's Report will deal with the effects of carbon monoxide in man and animals. While carbon monoxide is normally produced in the body, the blood carboxyhaemoglobin concentration rises as a result of inhaling cigarette smoke. Although the epidemiological evidence suggests that tobacco smoke is associated with a number of types of cardiovascular disease, we have found the evidence to indicate that carbon monoxide is the principal factor to be less than convincing. Nevertheless, there is evidence that exposure to carbon monoxide can affect cardiac electrical activity and in some people may affect myocardial function. There is also clear evidence that it may enhance the onset of symptoms of angina pectoris in those already at risk. The possible interaction of monoxide with other potentially noxious components in smoke should not be ignored. The exposure of animals to smoke and carbon monoxide has yielded conflicting data on the development of atherosclerosis, and further studies are needed.

9 The carbon monoxide yields of cigarettes determined by the Laboratory of the Government Chemist between December 1978 and June 1979 varied between 0.6 and 21.5 mg/cigarette for brands in the UK with annual sales of 10 million or more. The mean yield of all filtered cigarette brands was 14.3 mg/cigarette and for all non-filtered brands was 12.5 mg/cigarette. It is the practice for the Laboratory of the Government Chemist and the tobacco industry to exchange scientific information. For carbon monoxide this has not happened, but I hope that this will take place

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shortly. The industry, in the absence of satisfactory techniques for removing carbon monoxide selectively, has used non-selective methods such as smoke dilution. Consequently it is only those cigarettes with highly porous paper and or/ventilated filters which are generally low in carbon monoxide.

10 The removal of carbon monoxide per se should not, in principle, affect the flavour characteristics of cigarettes. But, in practice, the non-selective methods which may be used may ultimately alter the relative yields of other constituents in smoke and thereby affect some measure of acceptability to the consumer. And it may be necessary to devise new methods in order to achieve further reductions in carbon monoxide yields. Nevertheless, in spite of these difficulties, we think that the industry should be asked to make substantial reductions in the carbon monoxide yield of its products and that no new brands should be introduced which have a carbon monoxide yield in excess of the current mean of 14 mg/cigarette for all brands on sale in the UK.

NICOTINE

11 The role and effect of nicotine in smoke are extremely complicated; it is likely to be the component responsible for dependence upon cigarette smoking and thought by some to be a contributing factor in the development of cardiovascular disease. The Committee is carrying out a comprehensive survey of the pharmacology and toxicology of nicotine. In our Second Report we commented on the interrelationship of 'tar' and nicotine yields of cigarettes. Until our review has been completed and evaluated, we recommend that the nicotine yield of cigarettes should gradually fall as 'tar' is reduced and that the nicotine yield of any new brand should not be above the current sales-weighted average of 1.3 mg/cigarette for all brands on sale in the UK.

RESEARCH

12 In the Second Report, my Committee said that it proposed to ask the industry to provide full relevant data to assist it in reviewing and evaluating those constituents. I can now report that as a result of subsequent discussions, the tobacco manufacturers have agreed to fund research in those areas which the Committee considers important. In addition to 'tar', nicotine and carbon monoxide as mentioned above, research should be undertaken to investigate other constituents of smoke which have been judged to, or suspected to contribute to the health hazards of smoking. The Committee will outline areas of research that will advance knowledge of smoke toxicology, which in turn may lead to less hazardous products.

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MONITORING

13 The Second Report also referred to the need, in the Committee's view, for long-term human health studies to assess the effects of cigarettes containing tobacco substitutes as well as those containing tobacco. We think that such studies are necessary to monitor the effects on human health of changes made to reduce the toxicity of cigarettes. I am pleased to report that all cigarette manufacturers in the UK have agreed to be advised by a panel of eminent scientists to be chaired in the first instance by Professor W W Holland, and that they would establish an independent research body to carry out the programme of research which that panel advises should be done.

14 Although the industry is willing to finance epidemiological studies, I must stress that the independence of the body must be clear to all: the members who will serve on it and the programme of work it will pursue will be decided by the chairman in conjunction with the Chief Scientific Adviser to the Independent Scientific Committee on Smoking and Health.

15 Finally, if you should decide to publish this letter, my Committee would, of course, have no objection.

I am, Gentlemen,
Your obedient Servant

Hunter of Newington

Sent to:

Secretary of State for Social Services
Secretary of State for Northern Ireland
Secretary of State for Scotland
Secretary of State for Wales

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